

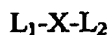
Application No. 09/732,241  
 Amendment Under 37 C.F.R. § 1.111 dated June 17, 2005  
 Reply to Office Action of May 23, 2005

PATENT  
 Attorney Docket No. P-095-US1  
 Customer No. 27038

### III. AMENDMENTS TO THE CLAIMS

This listing of the claims will replace all prior versions, and listings, of claims in the application.

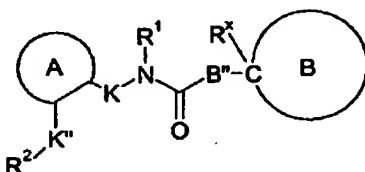
1. (Currently Amended) A compound of Formula (I):



(I)

wherein:

$L_1$  is a group of formula (a):



(a)

wherein:

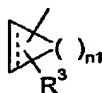
A is an aryl or a heteroaryl ring;

$B''$  is -O-;

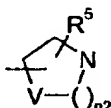
$R^x$  is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, acyl, acylamino, aminoacyloxy, aryl, carboxyalkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, ~~substitutes~~ substituted cycloalkenyl, heteroaryl, heteroaralkyl, alkylsulfonyl, or alkylsulfinyl;

$R^1$  is hydrogen or alkyl;

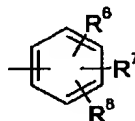
$R^2$  is Het, or is selected from [a] the group consisting of formula (i), (ii), and (iii):



(i)



(ii)



(iii)

wherein:

----- is an optional double bond;

$n_1$  is an integer of from 1 to 4;

$n_2$  is an integer of from 1 to 3;

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V is  $-\text{CH}-$ ,  $-\text{O}-$ ,  $-\text{S}(\text{O})_{n_3}-$ ,  $-\text{S}(\text{O})_{n_3}-$  (where  $n_3$  is an integer of from 0 to 2), or  $-\text{NR}^4-$  (wherein  $\text{R}^4$  is hydrogen, alkyl, substituted alkyl, aryl, or heteroaryl);

"Het" is a heteroaryl ring which optionally attaches a the group of formula (a) to X a linker;

$\text{R}^3$  is hydrogen, alkyl, halo, amino, substituted amino,  $-\text{OR}^a$  (where  $\text{R}^a$  is hydrogen, alkyl, or acyl), or a covalent bond attaching a the group of formula (a) to X a linker;

$\text{R}^5$  is hydrogen, alkyl, halo, amino, substituted amino,  $-\text{OR}^b$  (where  $\text{R}^b$  is hydrogen or alkyl), aryl, aralkyl, heteroaralkyl, or a covalent bond attaching a the group of formula (a) to X a linker;

$\text{R}^6$ ,  $\text{R}^7$ , and  $\text{R}^8$  are, independently of each other, hydrogen, halo, hydroxy hydroxyl, alkoxy, haloalkoxy, ~~carboxy~~ carboxyl, alkoxycarbonyl, alkyl optionally substituted with one, two or three substituents selected from halo, hydroxy hydroxyl, ~~carboxy~~ carboxyl, alkoxycarbonyl, alkylthio thioalkoxy, alkylsulfonyl, amino, substituted amino, or a covalent bond attaching a the group of formula (a) to X a linker;

K is a bond or an alkylene group;

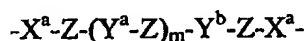
K" is a bond,  $-\text{C}(\text{O})-$ ,  $-\text{S}(\text{O})_{n_4}-$  (where  $n_4$  is an integer of from 0 to 2), or an alkylene group optionally substituted with a hydroxyl group; and

B is heterocycloamino or heteroarylamino, which optionally attaches a the group of formula (a) to X a linker;

provided that at least one of the  $\text{R}^3$ ,  $\text{R}^5$ ,  $\text{R}^6$ ,  $\text{R}^7$ ,  $\text{R}^8$ , "Het", heterocycloamino, or heteroarylamino groups attaches a the group of formula (a) to X a linker;

$\text{L}_2$  is an organic group comprising at least one primary, secondary or tertiary amine; and

X is a linker of has the formula:



wherin

$m$  m is an integer of from 0 to 20;

$\text{X}^a$  at each separate occurrence is selected from the group consisting of  $-\text{O}-$ ,  $-\text{S}-$ ,  $-\text{NR}-$ ,  $-\text{C}(\text{O})-$ ,  $-\text{C}(\text{O})\text{O}-$ ,  $-\text{C}(\text{O})\text{NR}-$ ,  $-\text{C}(\text{S})-$ ,  $-\text{C}(\text{S})\text{O}-$ ,  $-\text{C}(\text{S})\text{NR}-$  or a covalent bond where R is as defined below;

Z at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted cycloalkylene, alkenylene, substituted

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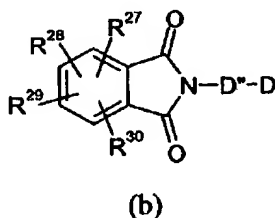
alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, and a covalent bond; and

$Y^a$  and  $Y^b$  at each separate occurrence are selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR-,  $-S(O)_n-$ ,  $-S(O)_n-$ , -C(O)NR'-, -NR' C(O)-, -NR' C(O)NR'-, -NR' C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)-NR'-, -NR'-C(O)-O-, -P(O)(OR')-O-, -O-P(O)(OR')-,  $-S(O)_nCR'R''-$ ,  $-S(O)_n-NR'-$ , -NR'-S(O) $_n$ -, -S-S-, and a covalent bond; where  $n$  is 0, 1 or 2; and R, R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocycle; provided at least one of  $X^a$ ,  $Y^a$ ,  $Y^b$  or Z is not a covalent bond;

or a pharmaceutically acceptable salt; or prodrug thereof.

2. (Currently Amended) The compound of claim 1 wherein  $L_2$  is a group selected from a the group consisting of:

(i) a group of formula (b):



wherein:

$D''$  is alkylene;

D is  $-NR^{31}R^{32}$ ,  $-N^+(R^{33}R^{34}R^{35})$  or  $-OR^{32}$  where  $R^{31}$ ,  $R^{33}$ , and  $R^{34}$  are, independently of each other, hydrogen, alkyl, or aralkyl; and  $R^{32}$  and  $R^{35}$  represent a covalent bond attaching a the group of formula (b) to X a linker;

$R^{27}$  is hydrogen, halo, nitro, cyano, hydroxy hydroxyl, alkoxy, ~~carboxy~~ carboxyl, alkoxycarbonyl, acyl, thio thiol, alkylthio thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy heteroaryloxy, heteroarylthio thioheteroaryloxy, heteroarylthio heterocycle, heterocyclyloxy heterocycloxy, aralkyl,

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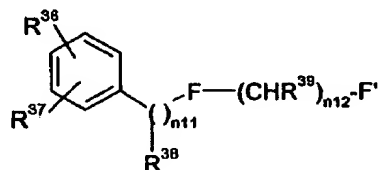
heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, ~~hydroxy~~ hydroxyl, ~~carboxy~~ carboxyl, alkoxycarbonyl, ~~alkylthio~~ thioalkoxy, alkylsulfonyl, amino, or substituted amino;

$R^{28}$  is hydrogen, halo, nitro, cyano, ~~hydroxy~~ hydroxyl, alkoxy, ~~carboxy~~ carboxyl, alkoxycarbonyl, acyl, ~~thio~~ thiol, ~~alkylthio~~ thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, or alkyl optionally substituted with one, two, or three substituents selected from halo, ~~hydroxy~~ hydroxyl, ~~carboxy~~ carboxyl, alkoxycarbonyl, ~~alkylthio~~ thioalkoxy, alkylsulfonyl, amino, or substituted amino;

$R^{29}$  and  $R^{30}$  are, independently of each other, hydrogen, alkyl, haloalkyl, halo, nitro, cyano, ~~hydroxy~~ hydroxyl, alkoxy, alkoxycarbonyl, acyl, ~~thio~~ thiol, ~~alkylthio~~ thioalkoxy, amino, mono- or dialkylamino; or

one of  $R^{27}$ ,  $R^{28}$ ,  $R^{29}$ , or  $R^{30}$  together with the adjacent group forms a methylenedioxy or ethylenedioxy group;

(ii) a group of formula (c):



(c)

wherein:

$n_{11}$  is an integer of from 1 to 7;

$n_{12}$  is 0 to 7;

F is  $\text{-NR}^{40}$ -,  $\text{-O-}$ ,  $\text{-S-}$ , or  $\text{-CHR}^{41}$ - (wherein  $R^{40}$  and  $R^{41}$  are, independently of each other, hydrogen, alkyl, or substituted alkyl);

$F''$  is a covalent bond,  $\text{-OR}^{43}$ ,  $\text{-NR}^{42}\text{R}^{43}$ , or  $\text{-N}^+\text{R}^{43}\text{R}^{44}\text{R}^{45}$  wherein  $R^{42}$  is hydrogen or alkyl,  $R^{44}$  and  $R^{45}$  are alkyl, and  $R^{43}$  is hydrogen, alkyl, or a covalent bond attaching a the group of formula (c) to X a linker;

$R^{36}$  is hydrogen, alkyl, halo, nitro, cyano, ~~hydroxy~~ hydroxyl, alkoxy, ~~carboxy~~ carboxyl, alkoxycarbonyl, acyl, ~~thio~~ thiol, ~~alkylthio~~ thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or

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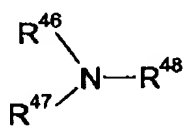
dialkylamino, aryl, aryloxy, arylthio, heteroaryl, ~~heteraryloxy~~ heteroaryloxy, ~~heterarylthio~~ thioheteroaryloxy, ~~heteroeyetyl~~ heterocycle, ~~heteroeyetyloxy~~ heterocycloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, ~~hydroxy~~ hydroxyl, ~~carboxy~~ carboxyl, alkoxycarbonyl, ~~alkylthio~~ thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R<sup>37</sup> is hydrogen, alkyl, halo, nitro, cyano, ~~hydroxy~~ hydroxyl, alkoxy, alkoxycarbonyl, acyl, ~~this~~ thiol, ~~alkylthio~~ thioalkoxy, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, ~~heteraryloxy~~ heteroaryloxy, ~~heterarylthio~~ thioheteroaryloxy, ~~heteroeyetyl~~ heterocycle, ~~heteroeyetyloxy~~ heterocycloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, ~~hydroxy~~ hydroxyl, ~~carboxy~~ carboxyl, alkoxycarbonyl, ~~alkylthio~~ thioalkoxy, alkylsulfonyl, amino, or substituted amino; and

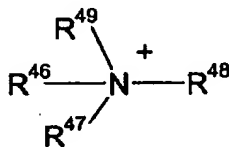
R<sup>38</sup> is hydrogen, alkyl, halo, ~~hydroxy~~ hydroxyl, alkoxy, or a covalent bond attaching the ligand to ~~X a linker~~ provided that at least one of R<sup>38</sup> and R<sup>43</sup> attaches a the group of formula (c) to X a linker;

R<sup>39</sup> is hydrogen, alkyl, halo, ~~hydroxy~~ hydroxyl, alkoxy, or substituted alkyl; and

(iii) a group of formula (d) or (e):



(d)



(e)

wherein:

R<sup>46</sup> is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, or heterocycle;

R<sup>47</sup> is alkyl, substituted alkyl, aryl, acyl, heterocycle, or -COOR<sup>50</sup> where R<sup>50</sup> is alkyl; or

R<sup>46</sup> and R<sup>47</sup> together with the nitrogen atom to which they are attached form a heterocycle, which heterocycle is optionally substituted with one or more alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, azido, cyano, ~~halogen~~ halo, hydroxyl, keto, thioketo, carboxyl, ~~carboxylalkyl~~ carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocycloxy, thiol, thioalkoxy, substituted thioalkoxy, aryl, aryloxy, heteroaryl,

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heteroaryloxy, ~~heterocyclic~~ heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, nitro,  
-SO-alkyl, -SO-substituted alkyl, -SO-aryl, -SO-heteroaryl, -SO<sub>2</sub>-alkyl, -SO<sub>2</sub>-substituted alkyl,  
-SO<sub>2</sub>-aryl or -SO<sub>2</sub>-heteroaryl;

R<sup>48</sup> is a covalent bond that attaches a the group of formula (d) to X a linker; and

R<sup>49</sup> is alkyl;

or a pharmaceutically acceptable salt; or prodrug thereof.

3. (Original) The compound of claim 1 or 2 wherein A is phenyl or pyridyl.
4. (Original) The compound of claim 1 or 2 wherein R<sup>1</sup> is hydrogen, methyl, or ethyl.
5. (Original) The compound of claim 1 or 2 wherein R<sup>2</sup> is pyrrolyl, pyridinyl, or imidazolyl.
6. (Original) The compound of claim 1 or 2 wherein R<sup>2</sup> is phenyl.
7. (Original) The compound of claim 1 or 2 wherein K is a bond or a methylene group.
8. (Original) The compound of claim 1 or 2 wherein K" is a bond.
9. (Original) The compound of claim 1 or 2 wherein R<sup>x</sup> is alkyl, alkenyl, or alkynyl, each optionally substituted with 1 to 5 alkoxy or fluoro substituents.
10. (Currently Amended) The compound of claim ~~1 or 2~~ 9 wherein R<sup>x</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl, (C<sub>2</sub>-C<sub>6</sub>)alkenyl, (C<sub>2</sub>-C<sub>6</sub>)alkynyl, each optionally substituted with 1 to 3 methoxy, ethoxy or fluoro substituents.
11. (Currently Amended) The compound of claim ~~1 or 2~~ 9 wherein R<sup>x</sup> is (C<sub>1</sub>-C<sub>6</sub>)alkyl optionally substituted with 1 to 3 methoxy, ethoxy, or fluoro substituents.
12. (Original) The compound of claim 1 wherein R<sup>x</sup> is methyl, ethyl, propyl, isopropyl,

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butyl, isobutyl or secbutyl, optionally substituted with methoxy or ethoxy or with 1 to 3 or fluoro substituents.

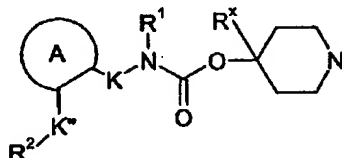
13. (Original) The compound of claim 1 wherein R<sup>x</sup> is methyl, ethyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, fluoromethyl, difluoromethyl, trifluoromethyl, trifluoromethoxymethyl, formyl, or acetyl.
14. (Original) The compound of claim 1 or 2 wherein R<sup>x</sup> is methyl, ethyl, methoxymethyl, fluoromethyl, difluoromethyl, or trifluoromethyl.
15. (Currently Amended) The compound of claim 1 or 2 wherein B is a heterocycloamino group which attaches a the group of formula (a) to X a-linker.
16. (Currently Amended) The compound of claim ~~1 or 2~~ 15 wherein B is pyrrolidine, piperidine, or hexahydroazepine attaching a the group of formula (a) to X a-linker.
17. (Currently Amended) The compound of claim ~~1 or 2~~ 16 wherein B is piperidine wherein the nitrogen atom of said piperidine attaches a the group of formula (a) to X a-linker.
18. (Currently Amended) The compound of claim ~~1 or 2~~ 16 wherein B is piperidin-3-yl or piperidin-4-yl wherein the nitrogen at the 1 position optionally attaches a the group of formula (a) to X a-linker.
19. (Original) The compound of claim 1 wherein B taken together with R<sup>x</sup> is 4-methylpiperidine-1,4-diyl.
20. (Original) The compound of claim 2 wherein L<sub>2</sub> is a group of formula (d) or (e).
21. (Previously Presented) The compound of claim 20 wherein: R<sup>46</sup> is alkyl or substituted alkyl; R<sup>47</sup> is alkyl, substituted alkyl, or heterocycle; or R<sup>46</sup> and R<sup>47</sup> together with the nitrogen atom to which they are attached form a heterocycle.

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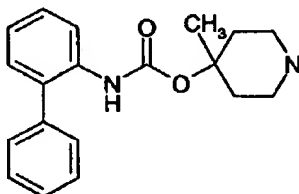
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22. Canceled.

23. (Original) The compound of claim 1 or 2 wherein  $L_1$  is:



24. (Original) The compound of claim 23 wherein  $L_1$  is:



25. (Currently Amended) The compound of claim 24 wherein the piperidino nitrogen of  $L_1$  is bonded attached to X.

26. (Previously Presented) The compound of claim 1 or 2 wherein X is alkylene optionally substituted with one, two, or three hydroxy groups, alkylene wherein one, two, or three carbon atoms have been replaced by an oxygen atom, or an -alkylene-phenylene-alkylene- wherein the phenylene ring is optionally substituted with one or two chloro or fluoro groups.

27. Canceled.

28. (Currently Amended) The compound of claim 1 or 2 wherein X is an alkylene group having from 3 to 20 carbon atoms; wherein one or more carbon atoms in the alkylene group is optionally replaced with -O-; and wherein the chain is optionally substituted on carbon with one or more hydroxyl groups.

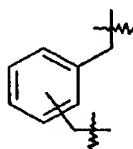


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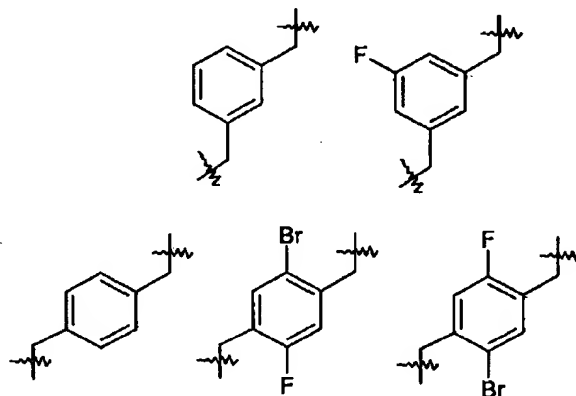
29. (Original) The compound of claim 1 or 2 wherein X is nonane-1,9-diyl, octane-1,8-diyl, propane-1,3-diyl, 2-hydroxypropane-1,3-diyl, or 5-oxa-nonane-1,9-diyl.

30. (Currently Amended) The compound of claim 1 or 2 wherein X has the following formula:

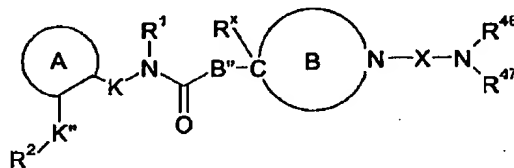


wherein the phenyl ring is optionally substituted with 1, 2, or 3 fluoro groups.

31. (Previously Presented) The compound of claim 1 or 2 wherein X has one of the following formulas:



32. (Currently Amended) The compound of claim 2 ~~which is a compound of~~ having Formula (Ia):



(Ia)

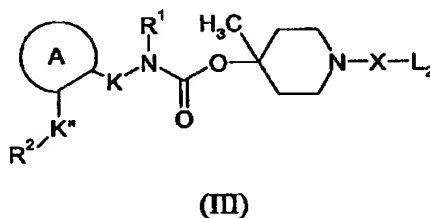
or a pharmaceutically acceptable salt or prodrug thereof.

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33. Canceled.

34. (Currently Amended) The compound of claim 1 ~~which is a compound of formula having~~  
Formula (III):



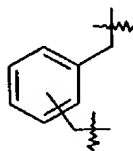
~~wherein  $R^2$ ,  $K^+$ , A, K,  $R^+$ , X, and  $L_2$  have the values defined in claim 1;~~ or a pharmaceutically acceptable salt or prodrug thereof.

35. Canceled.

36. (Currently Amended) The compound of claim 34 wherein X is an alkylene group having from 3 to 20 carbon atoms; wherein one or more carbon atoms in the alkylene group is optionally replaced with -O-; and wherein the chain is optionally substituted on carbon with one or more hydroxyl groups.

37. (Original) The compound of claim 34 wherein X is nonane-1,9-diyl, octane-1,8-diyl, propane-1,3-diyl, 2-hydroxypropane-1,3-diyl, or 5-oxa-nonane-1,9-diyl.

38. (Original) The compound of claim 34 wherein X has the following formula:

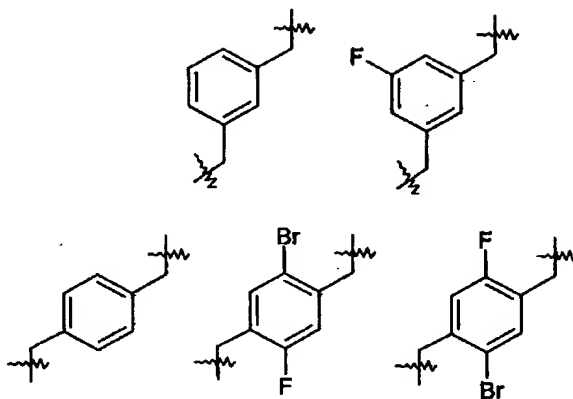


wherein the phenyl ring is optionally substituted with 1, 2, or 3 fluoro groups.

39. (Previously Presented) The compound of claim 34 wherein X has one of the following formulas:

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40. (Currently Amended) The compound of claim 2 20 wherein  $L_2$  is a group of formula (d) wherein  $R^{46}$  is a heterocycle, optionally substituted with 1 to 5 substituents independently selected from the group consisting of alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl; and  $R^{47}$  is alkyl, substituted alkyl, acyl, or  $-\text{COOR}^{50}$ .

41. (Currently amended) The compound of claim 2 20 wherein  $L_2$  is a group of formula (d) wherein  $R^{46}$  is alkyl that is optionally substituted with from 1 to 5 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, ~~halogen halo~~, hydroxyl, keto, thioketo, ~~carboxylalkyl~~ carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocycloxy, thiol, thioalkoxy, substituted thioalkoxy, ~~heterocycle~~ heterocycle, heterocycloxy, hydroxyamino, alkoxyamino, and  $\text{NR}^a\text{R}^b$ , wherein  $R^a$  and  $R^b$  may be the same or different [and] and are chosen from hydrogen, alkyl, substituted alkyl, cycloalkyl, alkenyl, cycloalkenyl, alkynyl, and ~~heterocycle~~ heterocycle.

42. (Currently amended) The compound of claim 2 20 wherein  $L_2$  is a group of formula (d) wherein  $R^{46}$  is 3-piperidinyl, 4-piperidinyl, or 3-pyrrolidinyl, which  $R^{46}$  is optionally substituted with 1 to 3 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, ~~halogen halo~~, hydroxyl, keto, thioketo, ~~carboxylalkyl~~ carboxyalkyl, thioaryloxy,

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thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, ~~heterocyclic~~  
heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, alkyl, substituted alkyl, alkenyl,  
substituted alkenyl, alkynyl, and substituted alkynyl.

43. (Currently amended) The compound of claim 2 20 wherein R<sup>46</sup> and R<sup>47</sup> together with the nitrogen atom to which they are attached form a piperidine or pyrrolidine ring which ring is optionally substituted with 1 to 3 substituents independently selected from the group consisting of alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, cyano, ~~halogen~~ halo, hydroxyl, keto, thioketo, ~~carboxylalkyl~~ carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocyclooxy, thiol, thioalkoxy, substituted thioalkoxy, ~~heterocyclic~~ heterocycle, heterocyclooxy, hydroxyamino, alkoxyamino, alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, and substituted alkynyl.

44. (Currently amended) The compound of claim 2 20 wherein R<sup>46</sup> and R<sup>47</sup> together with the nitrogen atom to which they are attached form a heterocycle that is an aza-crown ether.

45. (Original) The compound of claim 44 wherein the aza-crown ether is 1-aza-12-crown-4, 1-aza-15-crown-5, or 1-aza-18-crown-6.

46. Canceled.

47. (Previously Presented) A pharmaceutical composition comprising a pharmaceutically acceptable carrier and a therapeutically effective amount of a compound of claim 1 or 2.

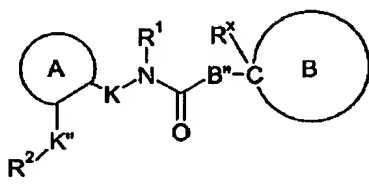
48. Canceled.

49. Canceled.

50. (Currently Amended) A compound of formula L<sub>1</sub>-H wherein L<sub>1</sub> ~~has the values defined in claim 1;~~ is a group of formula (a):

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(a)

wherein:

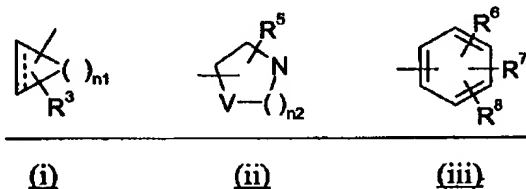
A is an aryl or a heteroaryl ring;

B'' is -O-;

R<sup>x</sup> is alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, acyl, acylamino, aminoacyloxy, aryl, carboxyalkyl, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, heteroaryl, heteroaralkyl, alkylsulfonyl, or alkylsulfinyl;

R<sup>1</sup> is hydrogen or alkyl;

R<sup>2</sup> is Het, or is selected from the group consisting of formula (i), (ii), and (iii):



wherein:

----- is an optional double bond;

n<sub>1</sub> is an integer of from 1 to 4;

n<sub>2</sub> is an integer of from 1 to 3;

V is -CH-, -O-, -S(O)<sub>n3</sub>- (where n<sub>3</sub> is an integer of from 0 to 2), or -NR<sup>4</sup>- (wherein R<sup>4</sup> is hydrogen, alkyl, substituted alkyl, aryl, or heteroaryl);

"Het" is a heteroaryl ring which optionally attaches the group of formula (a) to the hydrogen in L<sub>1</sub>-H;

R<sup>3</sup> is hydrogen, alkyl, halo, amino, substituted amino, -OR<sup>a</sup> (where R<sup>a</sup> is hydrogen, alkyl, or acyl), or a covalent bond attaching the group of formula (a) to the hydrogen in L<sub>1</sub>-H;

R<sup>5</sup> is hydrogen, alkyl, halo, amino, substituted amino, -OR<sup>b</sup> (where R<sup>b</sup> is hydrogen or alkyl), aryl, aralkyl, heteroaralkyl, or a covalent bond attaching the group of formula (a) to the hydrogen in L<sub>1</sub>-H;

R<sup>6</sup>, R<sup>7</sup>, and R<sup>8</sup> are, independently of each other, hydrogen, halo, hydroxyl, alkoxy,

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haloalkoxy, carboxyl, alkoxycarbonyl, alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxycarbonyl, thioalkoxy, alkylsulfonyl, amino, substituted amino, or a covalent bond attaching the group of formula (a) to the hydrogen in L<sub>1</sub>-H:

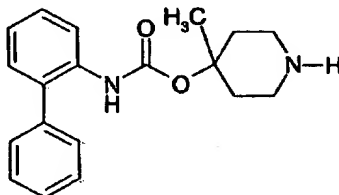
K is a bond or an alkylene group;

K" is a bond, -C(O)-, -S(O)<sub>n4</sub>- (where n<sub>4</sub> is an integer of from 0 to 2), or an alkylene group optionally substituted with a hydroxyl group; and

B is heterocycloamino or heteroarylamino, which optionally attaches the group of formula (a) to the hydrogen in L<sub>1</sub>-H;

provided that at least one of the R<sup>3</sup>, R<sup>5</sup>, R<sup>6</sup>, R<sup>7</sup>, R<sup>8</sup>, "Het", heterocycloamino, or heteroarylamino groups attaches the group of formula (a) to the hydrogen in L<sub>1</sub>-H; or a salt thereof.

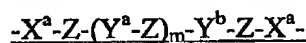
51. (Currently Amended) The compound of claim 50 ~~which is a compound of having~~ formula (V):



(V)

or a salt thereof.

52. (Currently Amended) A compound of formula R<sub>a</sub>-X-L<sub>2</sub> wherein X ~~and~~ has the formula:



wherein

m is an integer of from 0 to 20;

X<sup>a</sup> at each separate occurrence is selected from the group consisting of -O-, -S-, -NR-, -C(O)-, -C(O)O-, -C(O)NR-, -C(S)-, -C(S)O-, -C(S)NR- or a covalent bond;

Z at each separate occurrence is selected from the group consisting of alkylene, substituted alkylene, cycloalkylene, substituted cycloalkylene, alkenylene, substituted

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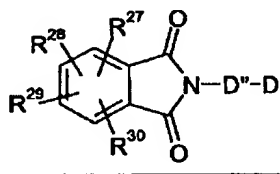
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alkenylene, alkynylene, substituted alkynylene, cycloalkenylene, substituted cycloalkenylene, arylene, heteroarylene, heterocyclene, and a covalent bond; and

Y<sup>a</sup> and Y<sup>b</sup> at each separate occurrence are selected from the group consisting of -O-, -C(O)-, -OC(O)-, -C(O)O-, -NR-, -S(O)<sub>n</sub>-, -C(O)NR'-, -NR' C(O)-, -NR' C(O)NR'-, -NR' C(S)NR'-, -C(=NR')-NR'-, -NR'-C(=NR')-, -OC(O)NR'-, -NR'-C(O)-O-, -P(O)(OR')-O-, -O-P(O)(OR')-, -S(O)<sub>n</sub>CR'R''-, -S(O)<sub>n</sub>-NR'-, -NR'-S(O)<sub>n</sub>-, -S-S-, and a covalent bond; where n is 0, 1 or 2; and R, R' and R'' at each separate occurrence are selected from the group consisting of hydrogen, alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, alkenyl, substituted alkenyl, cycloalkenyl, substituted cycloalkenyl, alkynyl, substituted alkynyl, aryl, heteroaryl and heterocycle; provided at least one of X<sup>a</sup>, Y<sup>a</sup>, Y<sup>b</sup> or Z is not a covalent bond;

L<sub>2</sub> have the values defined in claim 2; is selected from the group consisting of:

(i) a group of formula (b):



(b)

wherein:

D'' is alkylene;

D is -NR<sup>31</sup>R<sup>32</sup>-, -N<sup>+</sup>(R<sup>33</sup>R<sup>34</sup>R<sup>35</sup>) or -OR<sup>32</sup> where R<sup>31</sup>, R<sup>33</sup>, and R<sup>34</sup> are, independently of each other, hydrogen, alkyl, or aralkyl; and R<sup>32</sup> and R<sup>35</sup> represent a covalent bond attaching the group of formula (b) to X;

R<sup>27</sup> is hydrogen, halo, nitro, cyano, hydroxyl, alkoxy, carboxyl, alkoxycarbonyl, acyl, thiol, thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, thioheteroaryloxy, heterocycle, heterocyclooxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxycarbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R<sup>28</sup> is hydrogen, halo, nitro, cyano, hydroxyl, alkoxy, carboxyl, alkoxycarbonyl, acyl, thiol, thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl,

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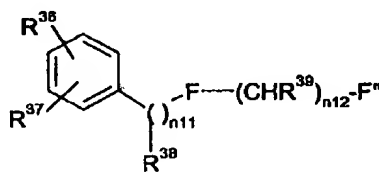
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thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, or alkyl optionally substituted with one, two, or three substituents selected from halo, hydroxyl, carboxyl, alkoxy, carbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R<sup>29</sup> and R<sup>30</sup> are, independently of each other, hydrogen, alkyl, haloalkyl, halo, nitro, cyano, hydroxyl, alkoxy, alkoxy carbonyl, acyl, thiol, thioalkoxy, amino, mono- or dialkylamino;  
or

one of R<sup>27</sup>, R<sup>28</sup>, R<sup>29</sup>, or R<sup>30</sup> together with the adjacent group forms a methylenedioxy or ethylenedioxy group;

**(ii) a group of formula (c):**



(c)

**wherein:**

$n_{11}$  is an integer of from 1 to 7;

$n_{12}$  is 0 to 7;

F is -NR<sup>40</sup>-, -O-, -S-, or -CHR<sup>41</sup>- (wherein R<sup>40</sup> and R<sup>41</sup> are, independently of each other, hydrogen, alkyl, or substituted alkyl);

F<sup>n</sup> is a covalent bond, -OR<sup>43</sup>, -NR<sup>42</sup>R<sup>43</sup>, or -N<sup>+</sup>R<sup>43</sup>R<sup>44</sup>R<sup>45</sup> wherein R<sup>42</sup> is hydrogen or alkyl, R<sup>44</sup> and R<sup>45</sup> are alkyl, and R<sup>43</sup> is hydrogen, alkyl, or a covalent bond attaching the group of formula (c) to X;

R<sup>36</sup> is hydrogen, alkyl, halo, nitro, cyano, hydroxyl, alkoxy, carboxyl, alkoxycarbonyl, acyl, thiol, thioalkoxy, alkylsulfonyl, alkylsulfinyl, sulfonamido, alkylsulfonamido, carbamoyl, thiocarbamoyl, mono or dialkylcarbamoyl, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy, thioheteroaryloxy, heterocycle, heterocycloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxycarbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino;

R<sup>37</sup> is hydrogen, alkyl, halo, nitro, cyano, hydroxyl, alkoxy, alkoxycarbonyl, acyl, thiol, thioalkoxy, amino, mono- or dialkylamino, aryl, aryloxy, arylthio, heteroaryl, heteroaryloxy,



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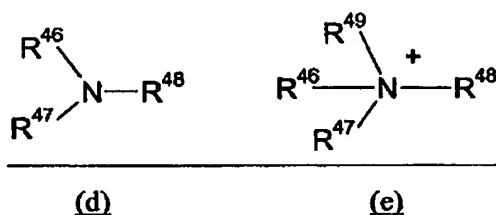
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thioheteroaryloxy, heterocycle, heterocycloxy, aralkyl, heteroaralkyl, or alkyl optionally substituted with one, two or three substituents selected from halo, hydroxyl, carboxyl, alkoxy, carbonyl, thioalkoxy, alkylsulfonyl, amino, or substituted amino; and

R<sup>38</sup> is hydrogen, alkyl, halo, hydroxyl, alkoxy, or a covalent bond attaching the ligand to X provided that at least one of R<sup>38</sup> and R<sup>43</sup> attaches the group of formula (c) to X;

R<sup>39</sup> is hydrogen, alkyl, halo, hydroxyl, alkoxy, or substituted alkyl; and

(iii) a group of formula (d) or (e):



wherein:

R<sup>46</sup> is alkyl, substituted alkyl, cycloalkyl, substituted cycloalkyl, or heterocycle;

R<sup>47</sup> is alkyl, substituted alkyl, aryl, acyl, heterocycle, or -COOR<sup>50</sup> where R<sup>50</sup> is alkyl; or

R<sup>46</sup> and R<sup>47</sup> together with the nitrogen atom to which they are attached form a heterocycle, which heterocycle is optionally substituted with one or more alkyl, substituted alkyl, alkenyl, substituted alkenyl, alkynyl, substituted alkynyl, alkoxy, substituted alkoxy, cycloalkyl, substituted cycloalkyl, cycloalkenyl, substituted cycloalkenyl, acyl, acylamino, acyloxy, amino, substituted amino, aminoacyl, aminoacyloxy, oxyaminoacyl, azido, cyano, halo, hydroxyl, keto, thioketo, carboxyl, carboxyalkyl, thioaryloxy, thioheteroaryloxy, thioheterocycloxy, thiol, thioalkoxy, substituted thioalkoxy, aryl, aryloxy, heteroaryl, heteroaryloxy, heterocycle, heterocycloxy, hydroxyamino, alkoxyamino, nitro, -SO-alkyl, -SO-substituted alkyl, -SO-aryl, -SO-heteroaryl, -SO<sub>2</sub>-alkyl, -SO<sub>2</sub>-substituted alkyl, -SO<sub>2</sub>-aryl or -SO<sub>2</sub>-heteroaryl;

R<sup>48</sup> is a covalent bond that attaches the group of formula (d) to X; and

R<sup>49</sup> is alkyl; and

R<sub>a</sub> is a suitable leaving group.